AMENDMENTS TO THE SPECIFICATION

Please replace paragraph [0039] with the following amended paragraph:

[0039] ~~FIG. 10 shows~~ Figs. 10A and 10B show coexpression in vitro of the hTRT and hTR to produce catalytically active human telomerase. Fig. 10A shows lane sets 1-4 and Fig. 10B shows lane sets 5-8.

Please replace paragraph [0051] with the following amended paragraph:

[0051] ~~FIG. 22 shows~~ Figs. 22A-D show the effect of mutation of the TRT gene in yeast. Fig. 22A shows the S. pombe trt1 locus and two deletion constructs; Fig. 22B shows telomere shortening in the trt1$^-$ mutant; Fig. 22C shows the colony morphology of trt1$^+$ and trt1$^-$ cells; and Fig. 22D are line drawings representing micrographs of trt1$^+$ and trt1$^-$ cells.

Please replace paragraph [0090] with the following amended paragraph:

[0090] In one aspect, the invention provides a polynucleotide having a sequence or subsequence of a human TRT gene or RNA. In one embodiment, the polynucleotide of the invention has a sequence of SEQ ID NO: 1, or a subsequence thereof. In another embodiment, the polynucleotide has a sequence of SEQ ID NO: 3 (FIG. 18), SEQ ID NO: 4 (FIG. 20), or subsequences thereof. The invention also provides polynucleotides with substantial sequence identity to the hTRT nucleic acid sequences disclosed herein, e.g., SEQ ID NO: 1 and any others disclosed (e.g., SEQ ID NOS: 4, 6 [FIG. 21], and 7 ~~[FIG. 22]~~). Thus, the invention provides naturally occurring alleles of human TRT genes and variant polynucleotide sequences having one or more nucleotide deletions, insertions or substitutions relative to an hTRT nucleic acid sequence disclosed herein. As described infra, variant nucleic acids may be produced using the recombinant or synthetic methods described below or by other means.

Please replace paragraph [0491] with the following amended paragraph:

[0491] To test S. pombe trt1 as a catalytic subunit, two deletion constructs were created. Fig. 22A. One removed only motifs B through D in the RT domains. The second removed 99% of the open reading frame.

Please replace paragraph [0492] with the following amended paragraph:

[0492] Haploid cells grown from S. pombe spores of both mutants showed progressive telomere shortening to the point where hybridization to telomeric repeats became almost undetectable. Fig. 22B. A $trt1^{+}/trt1^{-}$ diploid was sporulated and the resulting tetrads were dissected and germinated on a yeast extract medium supplemented with amino acids (a YES plate, Alfa, (1993) Experiments with Fission Yeast, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y.). Colonies derived from each spore were grown at 32°C. for three days, and streaked successively to fresh YES plates every three days. A colony from each round was placed in six ml of YES liquid culture at 32°C. and grown to stationary phase. Genomic DNA was prepared. After digestion with ApaI, DNA was subjected to electrophoresis on a 2.3% agarose gel, stained with ethidium bromide to confirm approximately equal loading in each lane, then transferred to a nylon membrane and hybridized to a telomeric DNA probe.

Please replace paragraph [0493] with the following amended paragraph:

[0493] Senescence was indicated by the delayed onset of failure to grow on agar (typically at the fourth streak-out after germination) and by colonies with increasingly ragged edges (colony morphology shown in FIG. ~~22B~~ 22C) and by increasingly high fractions of elongated cells (as shown in FIG. ~~22C~~ 22D). Cells were plated on Minimal Medium (Alfa (1993) supra) with glutamic acid substituted for ammonium chloride for two days at 32°C prior to photography.

Please replace paragraph [0614] with the following amended paragraph:

[0614] The results of the reconstitution are shown in ~~FIG. 10~~ Figs. 10A and 10B. For each transcription/translation reaction there are 3 lanes (a "lane set"): The first 2 lanes are duplicate assays and the third lane is a heat denatured (95°C., 5 min) sample to rule out PCR generated artifacts.

Please replace paragraph [0615] with the following amended paragraph:

[0615] As shown in ~~FIG. 10~~ Figs. 10A and 10B, reticulocyte lysate alone has no detectable telomerase activity (lane set 6). Similarly, no detectable activity is observed when either hTR alone (lane set 1) or full length hTRT gene (lane set 4) are added to the lysate. When both components are added (lane set 2), telomerase activity is generated as demonstrated by the characteristic repeat ladder pattern. When the carboxy-terminal region of the hTRT gene is removed by digestion of the vector with NcoI ("truncated hTRT") telomerase activity is abolished (lane set 3). Lane set 5 shows that translation of the truncated hTRT also did not generate telomerase activity. Lane "R8" shows a positive control (TSR8 quantitation standard (SEQ ID NO:329) (5'-ATTCCGTCGAGCAGAGTTAG[GGTTAG]7-3')).